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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Paper No. _____

Application Number: 09/954,975

Filing Date: September 18, 2001

Appellant(s): STAPLETON ET AL.

Steven L. Highlander
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed, September 29, 2003, and supplemental appeal brief, filed, December 8, 2003.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct.

(7) *Grouping of Claims*

Appellant's brief includes a statement that claims 31, 32, 35 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8), as such, Claims 11-30, 34,36-40 stand or fall together with claims 31, 32 and 35 being separately grouped.

(8) *ClaimsAppealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

5,093,134	Murrer et al.	3-1992
5,525,598	Collery et al.	6-1996
5,883,088	Bernstein	3-1999

File CANCERLIT, STN/CAS online, Acc. No. 94690969, Doc. No. 94690969

(Narasimhan, "The effect of copper and gallium compounds on ribonucleotide reductase", Dis. Abstr. Int. [B] (1993), Vol. 53, No. 10, p. 5114), Abstract. A full text version is attached as Exhibit A.

Acknowledged Prior Art, Specification, p. 2, lines 15-24, 27-29, p. 3, lines 8-20.

(10) *Grounds of Rejection*

Claims 11-13, 16-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murrer et al. (US Pat. 5,093,134) in view of the acknowledged prior art and Narasimhan. This rejection is set forth in prior Office Action, Paper No. 4/23/2003.

Claims 11-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over the acknowledged prior art in view of Narasimhan, Collery et al. (US Pat. 5,525,598) and Bernstein (US Pat. 5,883,088). This rejection is set forth in prior Office Action, Paper No. 4/23/2003.

(11) *Response to Argument*

Examiner acknowledges Applicant's statement regarding the proper standard of review and requirements for a valid *prima facie* case. Examiner notes that the rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally

available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. In re Fine, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 21 USPQ2d 1941 (Fed. Cir. 1992). See also In re Kotzab, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000) (setting forth test for implicit teachings); In re Nilssen, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988) (references do not have to explicitly suggest combining teachings); and Ex parte Levengood, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993) (reliance on logic and sound scientific reasoning).

Claims 11-13, 16-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murrer et al. (US Pat. 5,093,134) in view of the acknowledged prior art and Narasimhan.

Although Applicant admits that Narasimhan discloses that gallium inhibits ribonucleotide reductase and gallium nitrate has been known to inhibit reverse transcriptase as early as 1974, Applicant argues that Narasimhan (Abstract) fails to mention anything regarding anti-viral applications, much less about HIV. (Examiner notes that the full text version at pg. 99 does disclose the ribonucleotide reductase is considered to be an attractive target enzyme for anti-viral drugs, however, said disclosure is not necessary to reach a conclusion that the prior art rejection meets the requirement of a *prima facie* case). Applicant concludes that the motivation to use gallium as an anti-HIV therapeutic must come from somewhere else.

The motivation is based on sound scientific reasoning and logic. Applicant acknowledges that current treatments include treatment with dideoxynucleotides, such as AZT, dideoxyinosine and dideoxycytidine (Specification, Pg. 2, lines 27-29). Applicant also acknowledges that inhibition of ribonucleotide reductase inhibits HIV replication and that ribonucleotide reductase inhibitors potentiate the activity of dideoxynucleotides which are

nucleoside reverse transcriptase inhibitors (Specification, Pg. 3, lines 8-20). Since gallium, as indicated above, inhibits both ribonucleotide reductase and reverse transcriptase, one of ordinary skill in the art would expect that gallium would be effective in inhibiting HIV.

Applicant admits that the Murrer et al. clearly addresses HIV therapies and that gallium is explicitly disclosed as being contained in two of the compounds tested for activity against HIV. Applicant argues that nothing in Murrer et al. suggests that gallium itself acts as an antiviral agent. However, Applicant's method claims only require that the gallium composition is present in an amount to inhibit HIV replication not that gallium itself act as an antiviral agent and Applicant's composition and kit claims do not mention antiviral activity. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, gallium is hardly non-critical or inconsequential. Murrer et al. discloses that the gallium containing compounds are effective in inhibiting HIV and are used to inhibit HIV and treat AIDS (See Murrer et al., Column 1, lines 1-47, Column 2, lines 18-50, Column 3, lines 12,13, Column 3, 4, Table, Column 4, lines 65-68, Column 4, lines 1-3, 7,8).

Applicant dismisses the rule that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references (See *In re Keller*, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 231 USPQ 375 (Fed. Cir. 1986)) as being unhelpful. However, the rule was laid down to prohibit the very types of arguments that Applicant is making, i.e. arguing each reference in isolation to the other references, including the acknowledged prior art. Applicant also dismisses the rule that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of

the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references (See *In re Keller*, 208 USPQ 871 (CCPA 1981)) as perplexing. The rule is hardly perplexing as it simply indicates that bodily incorporation of the features of the secondary reference in the primary reference is not required and that each reference is not required to explicitly disclose the combination of each component or explicitly disclose the entire claimed invention. Applicant argues that it has argued nothing of the sort. However, as indicated above, Applicant has argued each reference in isolation with the other references, including the acknowledged prior art, i.e. indicating that Narasimhan fails to mention one or more features and that Murrer et al. fails to mention one or more features. What Applicant fails to address is the combination of Murrer et al. in view of the acknowledge prior art and Narasimhan.

Contrary to Applicant's arguments, Examiner has addressed the likelihood of success in inhibiting HIV *in vivo*. As indicated above, gallium containing compounds are disclosed to suitable for use *in vivo* in the treatment of HIV and AIDS, gallium is disclosed to inhibit ribonucleotide reductase and reverse transcriptase and inhibition of the same is disclosed to inhibit HIV. As such, one of ordinary skill in the art would expect that gallium would inhibit HIV *in vivo*. Applicant's argument that *in vitro* evidence is insufficient to even begin to address whether gallium can inhibit HIV in a human subject is without merit. Obviousness does not require absolute predictability, only a reasonable expectation of success, i.e., a reasonable expectation of obtaining similar properties. See, e.g., *In re O 'Farrell*, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). This is not a case where the prior art provides a general approach that seemed a promising field of experimentation or general guidance as to the particular form of the claimed invention or how to achieve. The prior art discloses a gallium composition which inhibits HIV

as well as a method of administering said gallium composition to humans for treatment of HIV and AIDS, including formulations, routes of administration and doses (See Murrer et al., Column 1, lines 1-47, Column 2, lines 18-50, Column 3, lines 12,13, Column 3, 4, Table, Column 4, lines 1,3,7,8, 60-68, Column 5, lines 10-20, Column 6, lines 3-14).

Claims 11-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over the acknowledged prior art in view of Narasimhan, Collery et al. (US Pat. 5,525,598) and Bernstein (US Pat. 5,883,088).

Contrary to Applicant's assertion, the acknowledged prior art is the primary reference. Further, as indicated above, the Narasimhan abstract is not required to indicate anti-viral applications (Examiner notes, as indicated above, that the full text version does mention anti-viral application but that the full text version is unnecessary to arrive at a *prima facie* case of obviousness herein).

Applicant admits that Collery et al. clearly describes the possibility of HIV therapies. Applicant, however, argues that Collery et al. that teaches away from the claimed invention. The mere fact that the gallium complexes are less effective than existing drugs such as AZT and that the patent claims were limited to use of these compounds in treating tumors do not constitute a teaching away from the claimed invention. "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). Further, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See *In re Susi*, 169 USPQ 423 (CCPA 1971).

Contrary to Applicant's arguments, the prior art discloses that gallium compositions are effective in inhibiting reverse transcriptase and inhibiting HIV and discloses formulations, routes of administration and doses for anti-viral treatment (Collery et al., Column 1, lines 28-33, Column 3, lines 20-58, Column 4, lines 1-5, Column 16, lines 5-28, Table VII). Further, as indicated above, Applicant also acknowledges that inhibition of ribonucleotide reductase inhibits HIV replication and that ribonucleotide reductase inhibitors potentiate the activity of dideoxynucleotides which are nucleoside reverse transcriptase inhibitors (Specification, Pg. 3, lines 8-20). Since gallium, as indicated above, inhibits both ribonucleotide reductase and reverse transcriptase, one of ordinary skill in the art would expect that gallium would be effective in inhibiting HIV.

As indicated above, Applicant's claims are directed to a gallium composition, as such, the inhibition of HIV by gallium in the context of N-heterocycles is clearly within the claim limitations. Further, the mere fact that the Narasimhan abstract is silent on treatments does not overcome the rejection herein. Again, the rules set forth in *Keller* and *Merck*, *supra*, are clearly relevant to the situation here where Applicant has argued against each prior art individually in isolation to the other prior art. As indicated above, absolute predictability is not required, only a reasonable expectation of success. Herein, the prior art discloses that gallium compositions are effective in inhibiting reverse transcriptase and ribonucleotide reductase and inhibiting HIV, that inhibition of reverse transcriptase and ribonucleotide reductase inhibits HIV and that gallium composition can be administered to humans for treatment of HIV, including formulation, routes of administration and doses (See acknowledged prior art, Specification, Pg. 2, lines 27-29, Pg. 3, lines 8-20; Narasimhan, Abstract; Collery et al., Column 1, lines 24-32, Columns 15,16, Table

VII). As such, one of ordinary skill in the art would expect that gallium would be effective in vivo to treat HIV infection.

Claims 31, 32 and 35 are not separately patentable.

Applicant argues that claims 31, 32 and 35 are separately patentable because the cited references do not teach reducing virus shed , viral burden and inhibiting development of AIDS, respectively. The claims, however, only require that an amount of gallium composition be administered to inhibit HIV replication. As indicated above, the prior art discloses that gallium compositions inhibit HIV, as such, one of ordinary skill in the art would expect that virus shed and viral burden would also be reduced. Further, Applicant acknowledges that infection of T-lymphocytes by HIV leads to the development of AIDS (Acknowledged prior art, Specification, pg. 2, lines 15-23; See also, Murrer et al., Column 1, lines 5-49 (compounds which inhibit HIV are indicated for treatment of AIDS; Collery et al., Column 3, lines 18-65, Column 4, lines 1-5 (gallium complexes screened for anti-HIV activity for indication as anti-AIDS drug). As such, since the prior art discloses that gallium compositions inhibit HIV, one of ordinary skill in the art would expect that administration of gallium compositions would inhibit the development of AIDS.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,



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May 14, 2004

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